UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/033,308	10/24/2001	M. Parameswara Reddy	2058-181	8198

22471 7590 09/29/2003

PATENT LEGAL DEPARTMENT/A-42-C
BECKMAN COULTER, INC.
4300 N. HARBOR BOULEVARD
BOX 3100
FULLERTON, CA 92834-3100

EXAMINER
BAKER, MAURIE GARCIA

ART UNIT	PAPER NUMBER
1639	9

DATE MAILED: 09/29/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.	Applicant(s)
10/033,308	Reddy et al
Examiner	**Art Unit**
Maurie G. Baker, Ph.D.	1639

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *THREE* MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☒ Responsive to communication(s) filed on *Jun 26, 2003* .

2a) ☒ This action is **FINAL.** 2b) ☐ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) *1-15, 18, and 20-25* is/are pending in the application.

4a) Of the above, claim(s) _____ is/are withdrawn from consideration.

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) *1-15, 18, and 20-25* is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9) ☐ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are a) ☐ accepted or b) ☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a) ☐ All b) ☐ Some* c) ☐ None of:

1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____ .
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

a) ☐ The translation of the foreign language provisional application has been received.

15) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s). _____
4) ☐ Interview Summary (PTO-413) Paper No(s). _____
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

1. The Response filed June 26, 2003 (Paper No. 8) is acknowledged. Claims 1-15 and 18 were amended, claims 16, 17 and 19 were cancelled and claims 20-25 were added. Therefore, claims 1-15, 18 and 20-25 are pending.

Status of Rejections

2. The rejection under 35 U.S.C. 112, second paragraph is withdrawn in view of applicant's claim amendments. However, all other rejections are maintained. Applicant's arguments are addressed following each rejection. Note that the maintained rejections may be slightly rewritten in light of the claim amendments and/or inclusion of the new claims therein.

Maintained Rejections
Claim Rejections - 35 USC § 102

3. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

4. Claims 1-4, 9-15, 18 and newly added 20 and 21 are rejected under 35 U.S.C. 102(b) as being anticipated by Stolowitz et al (WO 87/06586).

Stolowitz et al disclose a method of reacting molecules with amine-containing, activated supports (see Abstract). Specifically, amine-containing supports of Stolowitz such as aminopropyl silica gel (see, e.g. Example 1 and also page 3, lines 14-18) read on the claimed solid support having at least one available amino group. These amino groups are activated using "N,N'-carbonyldiimidazole (CDI) or a related azolide" (see page 3, lines 18-20). These read on the claimed activating compound having the structure L_1 –X– L_2 where X is a carbonyl and L_1 and L_2 are azole rings. Applicant's specifically elected species is disclosed by the reference on page 10, line 5. This reads directly on the instant claims 2-4 and 13-15. The reference discloses reacting the activated supports with amine containing compounds, see page 3, lines 21-26. In Example 1 of Stolowitz et al, glycine is reacted with an activated support. Glycine reads on the claimed biological molecule having at least one reactive amino group. The activation occurs in methylene chloride with triethylamine added, reading directly on instant claims 9 and 10 (see, e.g. Example 1, lines 8-11). The support is washed after activation, reading on instant claim 18 and newly added claim 21 (see, e.g. Example 1, lines 14-16). The coupling (in Example 1 of glycine, lines 16-18) is performed in a sodium carbonate buffer, reading on instant claim 11.

Note that the supports of Stolowitz et al (i.e. aminopropyl silica gel or controlled pore glass; see page 3, lines 14-18) read on the newly added limitation of "bead" and glycine reads on the newly added limitation of polypeptide, as defined by applicant on page 4, lines 25-26 of the instant specification.

Response to Arguments

5. Applicant's arguments filed June 26, 2003 have been fully considered but are not found persuasive. The examiner's rationale is set forth below.

6. It is first noted for the record that applicant argues the claims *as amended* in the Response filed June 26, 2003. Applicant argues that glycine, disclosed in Stolowitz et al, does not read on the now claimed biological molecule of oligonucleotide, nucleic acid, polypeptide or carbohydrate. The examiner respectfully disagrees. On page 4, lines 25-26 of the instant specification, applicant defines polypeptide as encompassing "proteins and antibodies, and any fragments thereof". As glycine is an amino acid and amino acids are fragments of proteins, this would read on the limitation of polypeptide.

7. Applicant also argues that Stolowitz et al does not disclose the now claimed solid support of bead, plate or film. However, applicant admits that Stolowitz et al discloses aminopropyl silica gel and controlled pore glass supports. These types of solid supports are commonly referred to in the art as "beads". A cursory search of the art reveals hundreds of documents that call these types of supports "beads". The examiner has included one of these references (i.e. Koster, US 6,300,076) to demonstrate this point. See column 12, lines 35-43 of Koster.

8. Thus, for these reasons and the reasons of record the above rejection under 35 U.S.C. 102(b) is maintained.

Maintained Rejections
Claim Rejections - 35 USC § 103

9. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

10. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

11. Claims 1-6, 9-15, 18 and newly added 20-23 and 25 are rejected under 35 U.S.C. 103(a) as being unpatentable over Stolowitz et al, as set forth above, in view of Milton (US 6,146,833; of record).

The teachings of Stolowitz et al are set forth *supra*. The reference teaches a method of reacting molecules with amine-containing, activated supports that reads on the claimed method.

Stolowitz et al lacks the specific teaching of depositing compounds in a particular area on the support (i.e. using printing). Stolowitz et al also lacks the specific teaching of the biological molecule being an oligonucleotide (new claim 25).

However, the use of printing techniques to deposit biological compounds onto solid supports was well established in the art at the time of filing, as evidenced by the teachings of Milton (see for example, column 12, lines 24-41). The reference teaches methods for printing compounds to make an array. See Examples 5 and 6 (note this procedure is *referred to in the instant specification*, pages 9 and 10). Milton specifically teaches the immobilization of e.g. oligonucleotides and peptides, see Examples 3-9 of the reference.

Therefore, it would have been *prima facie* obvious to one of ordinary skill in the art at the time of the invention to use the chemistry of Stolowitz et al for the activation of a amine-containing support for reaction with an amine compound in an array-type format using printing to deliver the amine compound (e.g. oligonucleotides or peptides) as taught by Milton. One of ordinary skill would have been motivated to do so due in order to create compounds "immobilized at site specific locations" as taught by Milton. One of ordinary skill would have had a high expectation of success as these printing techniques were well established in the art at the time of filing.

Response to Arguments

12. Applicant's arguments filed June 26, 2003 have been fully considered but are not found persuasive. The examiner's rationale is set forth below.

13. It is first noted for the record that applicant argues the claims *as amended* in the Response filed June 26, 2003. Applicant again states that Stolowitz et al does not teach the newly added limitations with respect to biological molecule and solid supports. The examiner's position is that the reference does disclose these elements, see paragraphs 5-8 above.

14. With respect to the combination of Stolowitz et al with Milton, applicant argues that there is no motivation, argues 'obvious to try' and also argues that there is a 'teaching away'. In response to applicant's argument that there is no suggestion to combine the references, the examiner recognizes that obviousness can only be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so found either in the references themselves or in the knowledge generally available to one of ordinary skill in the art. See *In re Fine*, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988) and *In re Jones*, 958 F.2d 347, 21 USPQ2d 1941 (Fed. Cir. 1992).

15. In this case, the examiner maintains that the *combined* teachings of the cited references render the claimed invention obvious. The teachings referred to in the

rejection are strong motivation. Note that the strongest rationale for combining references is a recognition, expressly or impliedly in the prior art or drawn from a convincing line of reasoning based on established scientific principles or legal precedent, that some advantage or expected beneficial result would have been produced by their combination. *In re Sernaker*, 702 F.2d 989, 994-95, 217 USPQ 1, 5-6 (Fed. Cir. 1983). In the instant case, the beneficial result of the combination of references is to create compounds "immobilized at site specific locations" as taught by Milton.

16. In response to applicant's argument that the rejection represents only an "obvious to try" rationale, the following from MPEP 2145 is noted:

> The admonition that obvious to try' is not the standard under § 103 has been directed mainly at two kinds of error. In some cases, what would have been obvious to try' would have been to vary all parameters or try each of numerous possible choices until one possibly arrived at a successful result, where the prior art gave either no indication of which parameters were critical or no direction as to which of many possible choices is likely to be successful. . . . In others, what was obvious to try' was to explore a new technology or general approach that seemed to be a promising field of experimentation, where the prior art gave only general guidance as to the particular form of the claimed invention or how to achieve it." In re O 'Farrell, 853 F.2d 894, 903, 7 USPQ2d 1673, 1681 (Fed. Cir. 1988) (citations omitted) (The court held the claimed method would have been obvious over the prior art relied upon because one reference contained a detailed enabling methodology, a suggestion to modify the prior art to produce the claimed invention, and evidence suggesting the modification would be successful.). See the cases cited in O 'Farrell for examples of decisions where the court discussed an improper "obvious to try" approach. See also In re Eli Lilly & Co., 902 F.2d 943, 14 USPQ2d 1741 (Fed. Cir. 1990) and In re Ball Corp., 925 F.2d 1480, 18 USPQ2d 1491 (Fed. Cir. 1991) (unpublished) for examples of cases where appellants argued that an improper "obvious to try" standard was applied, but the court found that there was proper motivation to modify the references.

The examiner's position is that the references ***do*** indicate which parameters are critical and ***do*** provide direction as to which of many possible choices is likely to be successful.

17. Lastly, applicant argues that the statement in Stolowitz et al that the invention "eliminates the {irreversible} adsorption of biological macromolecules and low

molecular weight amines observed with bonded phase supports which are not further derivatized" is a teaching away. The examiner does not understand this argument, as it appears that applicant has taken this statement completely out of context. The statement in the reference is referring to the performance of their derivatized bonded phase supports compared to un-derivatized supports of the prior art with respect to irreversible adsorption. This is a common problem in the chromatographic art. However, this has *absolutely nothing* to do with the teachings of the reference that pertain to the instant claims. As stated in the rejection, Stolowitz et al disclose a method of reacting molecules with amine-containing, activated supports (see Abstract). Thus, the relevant portions of Stolowitz et al are the portions that describe the *synthesis* of their derivatized bonded phase supports. These supports are made by covalently attaching a molecule (i.e. glycine) to a support and are particularly referred to in the rejection.

18. Thus, for these reasons and the reasons of record the above rejection under 35 U.S.C. 103(a) is maintained.

19. Claims 1-15, 18 and newly added 20-25 are rejected under 35 U.S.C. 103(a) as being unpatentable over Stolowitz et al, as set forth above, in view of Milton (US 6,146,833; of record), Okamoto et al (US 6,476,215) and Guo et al (Nuc. Acids Res. 1994, pp. 5456-5465).

The teachings of Stolowitz et al are set forth *supra*. The reference teaches a method of reacting molecules with amine-containing, activated supports that reads on the claimed method.

Stolowitz et al lacks the specific teaching of depositing compounds in a particular area on the support (i.e. using printing) and of using a humid chamber.

However, the use of printing or spotting techniques to deposit biological compounds onto solid supports was well established in the art at the time of filing, as evidenced by the teachings of all of Milton, Guo and Okamoto. The references all teach methods for spotting or printing compounds to make an array. See Milton, column 12, lines 24-41 and Examples 5 & 6 (note this procedure is referred to in the instant specification, pages 9 and 10); Guo et al, page 5457, 1st column; and Okamoto et al, columns 1-3.

Moreover, Guo and Okamoto teach using a humid chamber during the attachment of the probes to their arrays. See Guo, page 5457, 1st column; and Okamoto et al, column 18, lines 42-46, for example. This step is used to complete the reaction and/or to incubate the arrays.

Therefore, it would have been *prima facie* obvious to one of ordinary skill in the art at the time of the invention to use the chemistry of Stolowitz et al for the activation of a amine-containing support for reaction with an amine compound in an array-type format using printing or spotting to deliver the amine compound (e.g. oligonucleotides or peptides) as taught by any of Milton, Guo and Okamoto. One of ordinary skill would have been motivated to do so due in order to create

compounds "immobilized at site specific locations" as taught by Milton (for example). Furthermore, it would have also been *prima facie* obvious to one of ordinary skill in the art at the time of the invention to use a humid chamber to complete the reaction and/or to incubate the arrays once created. These techniques were also well established in the art as taught by Guo and Okamoto. One of ordinary skill would have had a high expectation of success as these printing and reaction techniques were well established in the art at the time of filing.

Response to Arguments

20. Applicant's arguments filed June 26, 2003 have been fully considered but are not found persuasive. The examiner's rationale is set forth below.

21. It is first noted for the record that applicant argues the claims *as amended* in the Response filed June 26, 2003. Applicant makes the same or similar arguments with respect to the disclosure of Stolowitz et al. Please see paragraphs 5-8 and 12-18 above.

22. Applicant also argues that "Milton, Guo and Okamoto do not teach or suggest "attaching" the biological molecule" (i.e. oligonucleotides, nucleic acids, polypeptides or carbohydrates) to a solid support (i.e. bead, plate or film). The examiner respectfully disagrees as each of these references clearly teaches *covalent attachment of a biological molecule to a solid support*, albeit by different chemistry than that which is claimed. See,

for example, Milton, column 3, lines 29-43 & scheme at the bottom of columns 9-10; Guo, Abstract ("oligonucleotides are covalently immobilized") & Figure 1; and Okamoto, column 5, line 38 – column 6, line 67. These references also clearly teach commonly used solid supports reading on beads, plates and/or films.

23. Thus, as stated in the rejection, since Stolowitz et al teaches the claimed attachment chemistry, it would have been *prima facie* obvious to one of ordinary skill in the art at the time of the invention to use the chemistry of Stolowitz et al for the activation of a amine-containing support for reaction with an amine compound in an array-type format using printing or spotting to deliver the amine compound (e.g. oligonucleotides or peptides) as taught by any of Milton, Guo and Okamoto for the reasons set forth in the rejection.

24. Thus, for these reasons and the reasons of record the above rejection under 35 U.S.C. 103(a) is maintained.

Status of Claims/ Conclusion

25. No claims are allowed.

26. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

27. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Maurie Garcia Baker, Ph.D. whose telephone number is (703) 308-0065. The examiner is on an increased flextime schedule but can normally be reached on Monday-Thursday and alternate Fridays from 9:30 to 7:00.

28. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Andrew J. Wang, can be reached at (703) 306-3217. The fax phone number for the organization where this application or proceeding is assigned is (703) 872-9306. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Maurie Garcia Baker, Ph.D.
September 23, 2003

MAURIE GARCIA BAKER PH.D
PRIMARY EXAMINER